CLAIMS

What is claimed is:

1. A purified and isolated seven transmembrane receptor polypeptide comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth in any one of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18 or 20, or a fragment thereof comprising an epitope specific to said seven transmembrane receptor polypeptide.

2. A purified and isolated seven transmembrane receptor polypeptide according to claim 1 comprising an amino acid sequence at least 90% identical to the amino acid sequence set forth in SEQ ID NO: 2, or a fragment thereof comprising an epitope specific to said seven transmembrane receptor polypeptide.

3. A purified and isolated seven transmembrane receptor polypeptide according to claim 1 comprising an amino acid sequence at least 90% identical to the amino acid sequence set forth in SEQ ID NO: 4, or a fragment thereof comprising an epitope specific to said seven transmembrane receptor polypeptide.

4. A purified and isolated seven transmembrane receptor polypeptide according to claim 1 comprising an amino acid sequence at least 90% identical to the amino acid sequence set forth in SEQ ID NO: 6, or a fragment thereof comprising an epitope specific to said seven transmembrane receptor polypeptide.

5. A purified and isolated seven transmembrane receptor polypeptide according to claim 1 comprising an amino acid sequence at least 90% identical to the amino acid sequence set forth in SEQ ID NO: 8, or a fragment thereof comprising an epitope specific to said seven transmembrane receptor polypeptide.

6. A purified and isolated seven transmembrane receptor polypeptide according to claim 1 comprising an amino acid sequence at least 90% identical to the amino acid sequence set forth in SEQ ID NO: 10, or a fragment thereof comprising an epitope specific to said seven transmembrane receptor polypeptide.

7. A purified and isolated seven transmembrane receptor polypeptide according to claim 1 comprising an amino acid sequence at least 90% identical to the amino acid sequence set forth in SEQ ID NO: 12, or a fragment thereof comprising an epitope specific to said seven transmembrane receptor polypeptide.

8. A purified and isolated seven transmembrane receptor polypeptide according to claim 1 comprising an amino acid sequence at least 90% identical to the amino acid sequence set forth in SEQ ID NO: 14, or a fragment thereof comprising an epitope specific to said seven transmembrane receptor polypeptide.

9. A purified and isolated seven transmembrane receptor polypeptide according to claim 1 comprising an amino acid sequence at least 90% identical to the amino acid sequence set forth in SEQ ID NO: 16, or a fragment thereof comprising an epitope specific to said seven transmembrane receptor polypeptide.

10. A purified and isolated seven transmembrane receptor polypeptide according to claim 1 comprising an amino acid sequence at least 90% identical to the amino acid sequence set forth in SEQ ID NO: 18, or a fragment thereof comprising an epitope specific to said seven transmembrane receptor polypeptide.

11. A purified and isolated seven transmembrane receptor polypeptide according to claim 1 comprising an amino acid sequence at least 90% identical to the amino acid sequence set forth in SEQ ID NO: 20, or a fragment thereof comprising an epitope specific to said seven transmembrane receptor polypeptide.

12. A purified and isolated seven transmembrane receptor polypeptide according to any one of claims 1-11.

13. A purified and isolated polypeptide according to any one of claims 1-11 comprising at least one extracellular domain of the seven transmembrane receptor polypeptide.

14. A purified and isolated polypeptide according to any one of claims 1-11 comprising the N-terminal extracellular domain of the seven transmembrane receptor polypeptide.

15. A purified and isolated polypeptide according to any one of claims 1-11 comprising a seven transmembrane receptor fragment selected from the group consisting of an N-terminal extracellular domain transmembrane domains, extracellular loops connecting transmembrane domains, intracellular loops connecting transmembrane domains, a C-terminal cytoplasmic domain, and fusions thereof.

16. A polypeptide according to any one of claims 1-15, wherein the polypeptide further includes a heterologous tag amino acid sequence.

17. A purified and isolated polynucleotide comprising a nucleotide sequence that encodes the polypeptide of claim 16.

18. A purified and isolated polynucleotide comprising a nucleotide sequence that encodes a polypeptide according to any one of claims 2, 3, 4, 8 or 9.

19. A purified and isolated polynucleotide comprising a heterologous expression control sequence operatively linked to a nucleotide sequence that encodes a polypeptide according to any one of claims 1-16.

20. The polynucleotide according to claim 19, wherein the expression control sequence is a promoter sequence that promotes expression of said polynucleotide in an eukaryotic cell.

21. The polynucleotide according to claim 19, wherein the promoter is a heterologous promoter that promotes expression of the polynucleotide in a human cell.

22. A purified and isolated polynucleotide comprising a nucleotide sequence that encodes a mammalian seven transmembrane receptor, wherein said polynucleotide hybridizes to any one of the nucleotide sequences set forth in SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, or 19 or the non-coding strand complementary thereto, under the following hybridization conditions:

(a) hybridization for 16 hours at 42°C in a hybridization solution comprising 50% formamide, 1% SDS, 1 M NaCl, 10% dextran sulfate and

(b) washing 2 times for 30 minutes at 60°C in a wash solution comprising 0.1x SSC and 1% SDS,

with the proviso that the nucleotide sequence of the polynucleotide differs from the coding sequence set forth in any one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, or 19 and from its complementary strand by at least one nucleotide.

23. A polynucleotide according to claim 22 that encodes a human seven transmembrane receptor.

24. A vector comprising a polynucleotide according to any one of claims 17-23.

25. A vector according to claim 24 that is an expression vector for expressing the polynucleotide in a mammalian cell.

26. A host cell stably transformed or transfected with a polynucleotide according to any one of claims 17-23 in a manner allowing the expression in said host cell of the polypeptide or fragment thereof encoded by the polynucleotide.

27. A host cell stably transformed or transfected with a vector according to claim 24 or 25 in a manner allowing the expression in said host cell of the polypeptide or fragment thereof encoded by the polynucleotide.

28. A method for producing a seven transmembrane receptor polypeptide comprising the steps of growing a host cell according to claim 26 or 27 in a nutrient medium under conditions in which the host cell expresses a seven transmembrane receptor encoded by the polynucleotide.

29. A method according to claim 28, further comprising a step of isolating said polypeptide from said cell or said medium.

30. A method according to claim 29, further comprising a step of isolating cell membranes from the host cell, wherein the cell membrane comprises the seven transmembrane receptor.

31. An antibody specific for a polypeptide according to any one of claims 1-15.

32. The antibody of claim 31 which is a monoclonal antibody.

33. A hybridoma that produces an antibody according to claim 32.

34. An antibody according to claim 31 that is a humanized antibody.

35. An antibody according to claim 31 that specifically binds an extracellular epitope of a seven transmembrane receptor having an amino acid sequence selected from the group consisting of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18 or 20.

36. An antibody according to claim 35 that specifically binds to the amino-terminal extracellular domain of the seven transmembrane receptors.

37. A cell-free composition comprising polyclonal antibodies, wherein at least one of said antibodies is an antibody according to claim 31.

38. An anti-idiotypic antibody specific for an antibody according to claim 31.

39. A polypeptide comprising a fragment of an antibody according to claim 31, wherein said fragment and said polypeptide specifically bind to a seven transmembrane receptor having an amino acid sequence selected from the group consisting of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18 or 20.

40. A polypeptide according to claim 39 that is selected from the group consisting of single chain antibodies and CDR-grafted antibodies.

41. A composition comprising a polypeptide according to any one of claims 1-16 in a pharmaceutically acceptable carrier.

42. A composition comprising an antibody according to any one of claims 31, 32, 34, 35, or 36, or a polypeptide according to claim 39 or 40, in a pharmaceutically acceptable carrier.

43. A method for modulating ligand binding of a seven transmembrane receptor polypeptide according to any one of claims 1-15, comprising the step of contacting said seven transmembrane receptor polypeptide with an antibody specific for said seven transmembrane receptor, under conditions wherein the antibody binds the receptor.

44. A method for modulating ligand binding of a seven transmembrane receptor polypeptide comprising the step of contacting said seven transmembrane receptor polypeptide with a polypeptide according to claim 39 or 40.

45. An assay to identify compounds that bind a seven transmembrane receptor polypeptide, said assay comprising the steps of:

(a) contacting a composition comprising a seven transmembrane receptor polypeptide according to any of claims 1-15 with a compound suspected of binding the seven transmembrane receptor polypeptide; and

(b) measuring binding between the compound and the seven transmembrane receptor polypeptide.

46. A method for identifying a modulator of binding between a seven transmembrane receptor polypeptide and a binding partner of the seven transmembrane receptor polypeptide, comprising the steps of:

(a) contacting the binding partner and a composition comprising the seven transmembrane receptor polypeptide in the presence and in the absence of a putative modulator compound, where the seven transmembrane receptor polypeptide is a polypeptide according to any one of claims 1-15;

(b) measuring binding between the binding partner and said seven transmembrane receptor polypeptide; and

(c) identifying a putative modulator compound in view of decreased or increased binding between the binding partner and seven transmembrane receptor polypeptide in the presence of the putative modulator, as compared to binding in the absence of the putative modulator.

47. An assay according to claim 45 or 46 wherein the composition comprises a cell expressing the seven transmembrane receptor polypeptide on its surface.

48. An assay according to claim 47 wherein the measuring step comprises measuring intracellular signaling of the seven transmembrane receptor polypeptide induced by the compound.

49. A method for treating a neurological disorder comprising the step of administering to a mammal in need of such treatment a pharmaceutical composition comprising a compound in an amount effective to modulate biological activity of a seven transmembrane receptor in neurons of said mammal, wherein the compound is selected from the group consisting of:

(a) an antibody according to any one of claims 31, 32, 34, 35, or 36;

(b) an anti-idiotypic antibody according to claim 38;

(c) a polypeptide according to claim 39 or 40;

(d) a compound identified according to the method of claim 45; and

(e) a modulator identified according to claim 46.

50. The method of claim 49 wherein the neurological disorder is schizophrenia.

51. A method according to claim 50, wherein the seven transmembrane receptor comprises a polypeptide according to claim 8.

52. A method of treating schizophrenia comprising the step of administering to a human diagnosed with schizophrenia an amount of a modulator of CON202 receptor activity sufficient to modulate CON202 receptor activity or CON202 ligand binding in said human.

53. A method of diagnosing schizophrenia or a susceptibility to schizophrenia comprising the steps of:

(a) measuring the presence or amount of expression or activity of a polypeptide according to claim 8 in a cell of a human patient: and

(b) comparing the measurement of step (a) to a measurement of expression or activity of the polypeptide in a cell from a normal subject or the patient at an earlier time. wherein the diagnosis of schizophrenia or susceptibility to schizophrenia is based on the presence or amount of CON202 polypeptide expression or activity.

54. A method of screening a human subject to diagnose a disorder affecting the brain or genetic predisposition therefor, comprising the steps of:

(a) assaying nucleic acid of a human subject to determine a presence or an absence of a mutation altering the amino acid sequence, expression, or biological activity of at least one seven transmembrane receptor that is expressed in the brain, wherein the seven transmembrane receptor comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, and 20, or an allelic variant thereof, and wherein the nucleic acid corresponds to the gene encoding the seven transmembrane receptor; and

(b) diagnosing the disorder or predisposition from the presence or absence of said mutation, wherein the presence of a mutation altering the amino acid sequence, expression, or biological activity of allele in the nucleic acid correlates with an increased risk of developing the disorder.

55. A method according to claim 54, wherein the seven transmembrane receptor is CON202 comprising an amino acid sequence set forth in SEQ ID NO: 14, or an allelic variant thereof.

56. A method according to claim 55, wherein the disease is schizophrenia.

57. A method according to claim 56, wherein the assaying step comprises at least one procedure selected from the group consisting of:

(a) determining a nucleotide sequence of at least one codon of at least one CON202 allele of the human subject;

(b) performing a hybridization assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences;

(c) performing a polynucleotide migration assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences; and

(d) performing a restriction endonuclease digestion to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences.

58. A method according to claim 56 wherein the assaying step comprises: performing a polymerase chain reaction (PCR) to amplify nucleic acid comprising CON202 coding sequence, and determining nucleotide sequence of the amplified nucleic acid.

59. A method of screening for a CON202 hereditary schizophrenia genotype in a human patient, comprising the steps of:

(a) providing a biological sample comprising nucleic acid from said patient, said nucleic acid including sequences corresponding to said patient's CON202 alleles;

(b) analyzing said nucleic acid for the presence of a mutation or mutations;

(c) determining a CON202 genotype from said analyzing step; and

(d) correlating the presence of a mutation in a CON202 allele with a hereditary schizophrenia genotype.

60. The method according to claim 59 wherein said biological sample is a cell sample.

61. The method according to claim 59 wherein said analyzing comprises sequencing a portion of said nucleic acid, said portion comprising at least one codon of said CON202 alleles.

62. The method according to claim 59 wherein said nucleic acid is DNA.

63. The method according to claim 59 wherein said nucleic acid is RNA.

64. A kit for screening a human subject to diagnose schizophrenia or a genetic predisposition therefor, comprising, in association:

(a) an oligonucleotide useful as a probe for identifying polymorphisms in a human CON202 seven transmembrane receptor gene, the oligonucleotide comprising 6-50 nucleotides that have a sequence that is identical or exactly complementary to a portion of a wild type human CON202 gene sequence or CON202 coding sequence, except for one sequence difference selected from the group consisting of a nucleotide addition, a nucleotide deletion, or nucleotide substitution; and

(b) a media packaged with the oligonucleotide containing information identifying polymorphisms identifyable with the probe that correlate with schizophrenia or a genetic predisposition therefor.

65. A method of identifying a seven transmembrane allelic variant that correlates with a mental disorder, comprising steps of:

(a) providing a biological sample comprising nucleic acid from a human patient diagnosed with a mental disorder, or from the patient's genetic progenitors or progeny;

(b) analyzing said nucleic acid for the presence of a mutation or mutations in at least one seven transmembrane receptor that is expressed in the brain, wherein the at least one seven transmembrane receptor comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, and 20, or an allelic variant thereof, and wherein the nucleic acid includes sequence corresponding to the gene or genes encoding the at least one seven transmembrane receptor;

(c) determining a genotype for the patient for the at least one seven transmembrane receptor from said analyzing step; and

(d) identifying an allelic variant that correlates with the mental disorder from the determining step.

66. A method according to claim 65, wherein the disorder is schizophrenia, and wherein the at least one seven transmembrane receptor comprises CON202 having an amino acid sequence set forth in SEQ ID NO: 14, or an allelic variant thereof.

67. A purified and isolated polynucleotide comprising a nucleotide sequence encoding a CON202 receptor allelic variant identified according to claim 66.

68. A host cell transformed or transfected with a polynucleotide according to claim 67 or with a vector comprising the polyncleotide.

69. A purified polynucleotide comprising a nucleotide sequence encoding a CON202 seven transmembrane receptor protein of a human that is affected with schizophrenia;

wherein said polynucleotide hybridizes to the complement of SEQ ID NO: 13 under the following hybridization conditions:

(a) hybridization for 16 hours at 42°C in a hybridization solution comprising 50% formamide, 1% SDS, 1 M NaCl, 10% dextran sulfate and

(b) washing 2 times for 30 minutes at 60°C in a wash solution comprising 0.1x SSC and 1% SDS; and

wherein the polynucleotide encodes a CON202 amino acid sequence that differs from SEQ ID NO: 14 at at least one residue.

70. A vector comprising a polynucleotide according to claim 69.

71. A host cell that has been transformed or transfected with a polynucleotide according to claim 70 and that expresses the CON202 protein encoded by the polynucleotide.

72. A host cell according to claim 71 that has been co-transfected with a polynucleotide encoding the CON202 amino acid sequence set forth in SEQ ID NO: 14 and that expresses the con202 protein having the amino acid sequence set forth in SEQ ID NO: 14.

73. A method for identifying a modulator of CON202 biological activity, comprising the steps of:

a) contacting a cell according to claim 71 in the presence and in the absence of a putative modulator compound;

b) measuring CON202 biological activity in the cell; and

c) identifying a putative modulator compound in view of decreased or increased CON202 biological activity in the presence versus absence of the putative modulator.

74. An assay to identify compounds useful for the treatment of schizophrenia, said assay comprising steps of:

(a) contacting a composition comprising a seven transmembrane receptor polypeptide according to claim 8 with a compound suspected of binding the seven transmembrane receptor polypeptide;

(b) measuring binding between the compound and the seven transmembrane receptor polypeptide; and

(c) identifying molecules that bind the seven transmembrane receptor as candidate compounds useful for the treatment of schizophrenia.

75. A method for identifying compound useful for a modulator of binding between a seven transmembrane receptor polypeptide and a binding partner of the seven transmembrane receptor polypeptide, which modulator is useful for treatment of schizophrenia, comprising the steps of:

(a) contacting the binding partner and a composition comprising the seven transmembrane receptor polypeptide in the presence and in the absence of a putative modulator compound, where the seven transmembrane receptor polypeptide is a polypeptide according to claim 8;

(b) measuring binding between the binding partner and the seven transmembrane receptor polypeptide;

(c) identifying a modulator compound useful for the treatment of schizophrenia in view of decreased or increased binding between the binding partner and seven transmembrane receptor polypeptide in the presence of the putative modulator, as compared to binding in the absence of the putative modulator.

76. An assay according to claim 74 or 75 wherein the composition comprises a cell expressing the seven transmembrane receptor polypeptide on its surface.

77. An assay according to claim 76 wherein the composition comprises a cell transformed or transfected with a polynucleotide encoding the seven transmembrane polypeptide and expressing the seven transmembrane receptor polypeptide on its surface.